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USSR SCIENTIST REPORTS ON 1955 WARSAW INTERNATIONAL
CONFERENCE ON ANTIBIOTICS

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An international conference on antibiotics was held in Warsaw 7-13 February 1955. Scientists from Bulgaria, Hungary, China, Korea, Poland, Rumania, the USSR, and Czechoslovakia participated in the conference. More than 30 reports were presented and discussed. These reports dealt principally with problems in two subdivisions: (1) the search for new antibiotics active against bacterial, fungal, and virus infections, and (2) the improvement of the effectiveness of available antibiotic preparations, i.e., of penicillin, streptomycin, aureomycin, and others. Many reports were devoted to the biology and systematization of organisms which produce antibiotics, their modifiability, and factors which modify their heredity considered from the standpoint of applications in the development of methods to obtain more active strains that form antibiotics. Problems connected with the chemical purification of antibiotics and their production were also discussed.

The conference was launched with a report by the Soviet delegation on new principles applied in the systematization, recognition, and differentiation of actinomycetes which produce antibiotics. This report pointed out the inadequacies from the standpoint of the differentiation of species of actinomycetes of the existing systems of classification which are based on external traits and physiological characteristics. More precise indexes are needed which make possible more exact differentiation. The Soviet microbiologists proposed that the phenomenon of antagonism and the specificity of this phenomenon be used as such indexes. The characteristics of the intraspecies and interspecies antagonistic actions of actinomycetes on each other and of the specificity of the activity of the antibiotics formed by them make it possible to differentiate between species and recognize among them with a considerable degree of exactitude known.

Great interest was elicited by a report presented by Professor Malek, Active Member of the Academy of Sciences of the Czechoslovak Republic. Professor Malek's report dealt with the directed modification of organisms producing antibiotics and with methods of modifying the heredity of these organisms. Malek emphasized the great significance of Michurin's teaching as a basis for studying the modifiability of microorganisms. By applying the method of disturbing the heredity with the aid of strongly acting agents and subsequently breeding the varieties which have been formed in this manner. Czechoslovak scientists succeeded in obtaining sufficiently active strains that form antibiotics (e.g., streptomycin).

Very interesting and detailed, as far as the scope of information given in them is concerned, were the reports by workers at the Laboratory of Antibiotics directed by Professor Kurylowicz (Warsaw). These reports dealt with the modifiability of actinomycetes which produce streptomycin (*Actinomyces globisporus streptomycini*), aureomycin (*A. aureofaciens*), and terramycin (*A. rimosus*) and also of the fungus *Penicillium chrysogenum*, which produces penicillin.

The Polish scientists have presented data which indicate that natural variants which are obtained without subjecting the microorganisms to any particular action and variants obtained under the action of strongly active influences (ultraviolet rays, X rays, yperite) do not differ among themselves in any essential respects as far as their antibiotic activity is concerned. For instance,

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out of 295 natural strains of *Actinomyces globisporus streptomycini*, several variants had a maximum activity amounting to 1,200 units per milliliter. The variants obtained by exposing the fungus to ultraviolet radiation had approximately the same activity.

Professor Horvat (Godollo, Hungary) gave an account of his observations on the subject of the transformation of some species of actinomycetes into other species by the method of vegetative hybridization. By culturing actinomycetes in an extract obtained from a culture of another species, he induced in the first species the characteristics of the second. He obtained the same results by culturing actinomycetes in a colony of an old autolized culture of another species.

Of interest were the communications dealing with the search for new antibiotics and the discovery of new antibiotics. Golanowska and Wrubel (Professor Ziminska's laboratory at Plawa) discussed the results obtained by them in searching for and isolating from the soil microbes which form antibiotics. They used the two-layer agar medium method which had been proposed by the Institute of Microbiology, Academy of Sciences USSR. Using a modification of this method, they selected a soil extract of a definite concentration which formed the basis for the substrate. As far as the frequency of occurrence and the regularities pertaining to the frequency of occurrence of microbe antagonists in the soil are concerned, these investigators noted the distinct influence exerted by the plants growing on the surface of the soil. The occurrence of antagonists and their species composition is also determined by the type of soil.

Milyanowicz (Professor Kurylowicz's Laboratory at Warsaw) presented a paper dealing with new methods of finding antagonists active against phages. The phages were used in this instance as models of viruses. The phages of *Bacterium coli*, of the typhoid bacillus (*B. typhi*) and of *B. proteus* X-19 were used. By applying her original method, this investigator isolated a number of phage antagonists among actinomycetes and mold fungi. Some of these antagonists exerted a depressing effect on animal viruses.

In a report of Kozinski (Chair of Microbiology, Warsaw Medical Institute) data were presented on a new method for the detection of antiviral antibiotics. This method is based on A. Carrel's method of tissue culture. As an object of investigation which is sensitive to the virus, a culture of cancer cells has been proposed that produces cancer in experimental animals and is rather widely used under the name Ge-Lya [sic]. When the antibiotic has been added to the substrate, the action of the virus is suppressed and the tissue culture continues to develop normally. Unless the positive effect described above takes place, the virus propagates profusely and poisons the cells, [so that the tissue culture does not develop]. It is recommended that this method be used in the search for antibiotics effective against the virus of poliomyelitis and other neurotropic viruses.

Woyciechowski (Institute of Hygiene, Warsaw) gave information on his method of determining the action of antibiotics on typhus rickettsiae. This method is based on the culturing of rickettsiae in the intestines of lice. By using the method in question, one may determine the action of antibiotics on the rickettsiae and also establish the therapeutic effect exerted by the antibiotics.

Professor Maizel (Warsaw) presented data dealing with the action of antibiotics on anaerobic bacteria which cause tetanus and gas gangrene. It has been found that penicillin and chloromycetin exert a bactericidal action on the vegetative cells of the anaerobes. Small doses of the antibiotics slow down the growth of the bacteria. They also bring about degeneration and an unusual type of development (involution). Reports were also presented on the mechanism of the effect exerted by streptomycin on biochemical processes.

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Professor Mikuljaszek (Chair of Microbiology, Warsaw Medical Institute) presented information on the action exerted by high-molecular compounds on plant and animal viruses. It has been established in the work described by Mikuljaszek that various reactions take place between the high-molecular compounds and the molecules of the viruses and that as a result of these reactions inactivation of the viruses is brought about. Methods of obtaining antiviral agents to be used for therapeutic purposes have been developed on this principle.

Professor Bogdasaryan (Warsaw) gave information on an over-all ["summation"] method of determining the propagation of microorganisms and the degree of assimilation by them. This method is based on determining the oxygen number, i.e., the total amount of oxygen which is necessary for the transformation of organic compounds into inorganic compounds forming the final products of metabolism.

Professor Gauze (Moscow) reported on a new antibiotic obtained in his laboratory, i.e., albomycin. This antibiotic is being subjected to extensive clinical tests at present.

Considerable attention was attracted by the reports presented by the delegation from the People's Republic of China. Wan Yuan (Shanghai) told about the use of cotton cake instead of corn extract in the production of penicillin. The data given in Wan Yuan's report are of great practical significance. Prof Chang Wei-shenq (Peiping) presented his experimental data on the role played by lactose and corn extract in the production of penicillin by fermentation induced by a culture of *P. chrysogenum*. Addition of lactose to the medium increases the yield of penicillin.

Engr Hsu Wen-Hsi (Shanghai) told about the production of aureomycin by fermentation and the obtaining of this antibiotic in a pure crystalline form. He developed completely the technology of producing this antibiotic starting with the growing of the producer organism (*Actinomyces aureofaciens*) in test tubes and ending with the fermentation in tissues.

Dr Popov (Bulgaria) cited very interesting experimental data on the production of antipenicillinase serum and its action. It is known that, as a result of the administration of antibiotics, resistant varieties of microorganisms originate in the bodies of patients. After a time, these microorganisms cease to react with the antibiotic in question, which thus loses its therapeutic effectiveness. The resistance of bacteria to penicillin is due to their capacity to form the enzyme penicillinase, which destroys the antibiotic. Bulgarian scientists have developed a method of neutralizing or reducing the action of penicillinase and, in this manner, depriving the bacteria of their protective characteristics. As a result, the bacteria's sensitivity to penicillin is restored. The scientists who worked on this problem established that penicillinase has antigenic properties. When penicillinase is introduced into the bodies of rabbits, antibodies (antipenicillinases) appear in the blood of the animals. The serum prepared from these antibodies counteracts the effect of penicillinase in the bodies of patients, so that the patients again begin to react positively to treatment with penicillin. The new preparation is being subjected to clinical tests.

Dr Skola (Czechoslovakia) reported on some results obtained in connection with the use of antibiotics in animal husbandry as stimulants of the growth of animals. Antibiotics were first used in Czechoslovakia for this purpose in 1951. Various antibiotics were tested; the best results were obtained with aureomycin and procaine-penicillin. Experiments on chickens resulted in an increase of weight amounting to 15%. Czechoslovak specialists (Gerold and Necasek) have developed a method of vitaminizing fodder. They introduced into the fodder appropriate microorganisms which, in the process of multiplication, formed vitamins. Such fodder is given to animals in a dilute state. The meat of animals to the food of which antibiotics have been added does not produce resistance as far as therapy with the antibiotics in question is concerned. The

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apprehension that humans who have used as food the meat of animals which have consumed antibiotics will be immunized to these antibiotics is not based on fact.

The report by the Hungarian scientist Professor Ivanovics concerning the phenomenon of the lysis of sporiferous bacteria was heard with great interest. This phenomenon reminds one of the effect produced by bacteriophages.

Among reports dealing with the chemistry of antibiotics, the greatest interest was elicited by papers of Kozytski, Vondracek, and Doskocil. Professor Kozytski (Warsaw) touched upon the problems of biogenesis and of the chemistry of antibiotics. He also discussed the structure of antibiotics and their classification. In his report, Professor Kozytski expressed his point of view concerning the mechanism of the formation of antibiotics by bacterial cells. In the report by Dr Vondracek (Czechoslovakia) dealing with experimental methods of isolating antibiotics, the fact was emphasized that at different stages of the production of antibiotics, different methods of isolation and purification are required. Czechoslovak specialists in this field used the combined method of adsorption on an active substrate or in ion-exchange equipment and extraction with an organic solvent. More often, the countercurrent principle and the method of precipitation are used. All these methods can be combined in various ways depending on the chemical and physical properties of the active substance to be isolated.

Dr Doskocil (Czechoslovakia) discussed the physicochemical analysis of antibiotics. Of the greatest interest in this field are the methods of polarography and oscillography of penicillin which have been developed in Czechoslovakia. Although penicillin does not exhibit any polarographic activity itself, one still could measure the polarographic wave of one of the products of the decomposition of penicillin in an acidic medium.

The conference pointed out the necessity of a close coordination of work and of an exchange of experience acquired by specialists active in various countries in work on different problems pertaining to antibiotics. The desire has been expressed to conduct regularly international conferences on antibiotics and to organize an international exchange of scientists; also to found an international review periodical and to publish a monograph on the subject. It has been decided to create a repository of living cultures of organisms which produce antibiotics and other metabolites and also of cultures to be used for standard tests as well as a collection of standardized preparations.

After the conference, the participants visited laboratories, institutes, and plants in Warsaw, the vicinity of Warsaw, and other cities of Poland. In Warsaw, they visited the Laboratory of Antibiotics of the Institute of Hygiene, the Antibiotics Plant, the Institute of Sera and Vaccines, the Chair and Laboratory of Microbiology of the Medical Institute, the Pharmaceutical Plant, the Pharmaceutical Institute, and the Laboratory of Dextran Production of the Institute of Food Industry. At Poznan, the participants at the conference visited the Laboratory of Agricultural Technology, where the antianemic vitamin B-12 is produced, and then the Chair of Plant Physiology of the university. At Wroclaw, the delegates to the conference inspected the Laboratory of Ion-Exchange Resins, the Chair of Physiological Chemistry of the Medical Academy, the Institute of Microbiology and Immunology of the Academy of Sciences of the Polish People's Republic, and the Institute of Pharmacological Chemistry of the Medical Academy. We, the participants at the conference, convinced ourselves that in Warsaw, Poznan, Wroclaw, and Krakow the plant laboratories are in an excellent state.

The Polish People's Republic has an extensive scientific research organization on which work in the field of biology is based. At various laboratories and institutes, work is conducted on a variety of biological problems, the

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majority of which have a close bearing on the practical needs of medicine, agriculture, and industry. Research on proteins is being successfully conducted in Poland. At Boronowski's Laboratory, Wroclaw, the structure of proteins is being investigated. At this laboratory, the existence of the protein myosin had been established for the first time. With the use of microbiological, biophysical, and chemical methods, the workers at this laboratory are successfully subjecting to study the proteins and amino acids of the blood and tissues of animals.

Of exceptional practical interest is the work which is being conducted on vitamin B-12 and dextran. Vitamin B-12 is being produced by the Laboratory of Agricultural Technology at Poznan with the aid of a culture of *Micobacterium propionicum*. The methods of growing the producer organism and of purifying the vitamin chemically are simple and easily carried out. The yield of vitamin is higher (up to 2 micrograms per milliliter) than in the production from actinomycetes, which yields 0.6-1.0 micrograms per milliliter.

Dextran, which is to be used as a blood substitute, is produced by special bacteria. This substance is manufactured at Warsaw by the Chemico-Pharmaceutical Institute in collaboration with the Institute of Food Industry.

One must point out one more achievement of Polish scientists, namely, a valuable chemical agent active against hypertension. This is an iodine derivative of barbituric acid which has been synthesized at the laboratory of the Chair of Pharmacology of the Medical Academy under the direction of Professor Bobranski. The new drug is being subjected to clinical tests.

At the Laboratory of Ion-Exchange Resins (Wroclaw), certain types of resins have been developed for the purification of active substances which are of value in the antibiotics industry. At one of the Wroclaw plants synthomycin is being produced. Vitamin C is being produced in large quantities. All this has convinced us that investigations in the field of antibiotics and work on the production of antibiotics and related products are being carried on in Poland on an extensive scale. The laboratories and institutes which are active there have the facilities for conducting their work in an efficient manner, so that valuable results are obtained.

The scientific community of Poland evinces a great interest toward research carried out in the USSR. Scientific books published in the USSR, i.e., monographs, textbooks, manuals, and reference books, are widely used at the laboratories and universities. There is a pronounced tendency to cooperate as closely as possible with Soviet scientists.

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